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which has been deleted from the claims is ~~struck-through~~. The Applicants have also enclosed a "Clean Copy of Claims, as Amended."

Applicants thank the Examiner for the withdrawal of objections and rejections, as described on page 2 of the present Office Action. Applicants also thank the Examiner for the allowance of claim 66, and for reporting at the bottom of page 5 of the Office Action that claims 2, 24, 25, 29, and 35 are objected to (and would be allowable is rewritten in independent form including all of the limitations of the base claim and any intervening claims).

Claims 1-7, 12, and 24-66 are pending following entry of this Amendment. Claims 1, 32, 33, 37, 39, 43, 44, 54, and 65 have been amended. The amendments made herein do not include new matter.

Please amend claims 1, 32, 33, 37, 39, 43, 44, 54, and 65 to read as follows.

1. (Amended Four Times) An isolated nucleic acid molecule, or its complement, wherein the isolated nucleic acid i) encodes a polypeptide which exhibits lipase activity and ii) is selected from the group consisting of:

El a) a nucleic acid molecule having a nucleotide sequence which is at least 90% identical to the nucleotide sequence of SEQ ID NO: 45 or 46;

b) a nucleic acid molecule comprising a fragment of SEQ ID NO: 45 or 46;

c) a nucleic acid molecule which encodes a polypeptide comprising the amino acid sequence encoded by SEQ ID NO: 46;

d) a nucleic acid molecule which encodes a fragment of the amino acid sequence encoded by SEQ ID NO: 46; and

e) a nucleic acid molecule which encodes a variant of the amino acid sequence encoded by SEQ ID NO: 46, wherein the nucleic acid molecule hybridizes over its full length in 6× sodium chloride/sodium citrate (SSC) at about 45°C, followed by one or more washes in 0.2×

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E¹ SSC, 0.1% SDS at 50°C with a portion of a nucleic acid molecule consisting of the nucleotide sequence of SEQ ID NO: 45 or 46.

E² 39. (Twice Amended) The isolated nucleic acid molecule of claim 1, or its complement, wherein the molecule hybridizes over its full length in 6× SSC at about 45°C, followed by one or more washes in 0.2× SSC, 0.1% SDS at 50°C with a nucleic acid molecule consisting of the nucleotide sequence of SEQ ID NO: 45 or 46.

E³ 33. (Twice Amended) The isolated nucleic acid molecule of claim 30, or its complement, wherein the nucleic acid molecule encodes a polypeptide comprising a fragment which comprises an immunogenic portion of the protein having the amino acid sequence encoded by SEQ ID NO: 46.

E⁴ 32. (Thrice Amended) The isolated nucleic acid molecule of claim 1, or its complement, wherein the nucleic acid molecule encodes a variant of the amino acid sequence encoded by SEQ ID NO: 46, wherein the nucleic acid molecule hybridizes over its full length in 6× SSC at about 45°C, followed by one or more washes in 0.2× SSC, 0.1% SDS at 50°C with a nucleic acid molecule consisting of the nucleotide sequence of SEQ ID NO: 45 or 46.

E⁵ 37. (Thrice Amended) The method of claim 12, wherein the polypeptide is a variant of the polypeptide encoded by SEQ ID NO: 46, wherein the polypeptide is encoded by a nucleic acid molecule which hybridizes over its full length in 6× SSC at about 45°C, followed by one or more washes in 0.2× SSC, 0.1% SDS at 50°C with a nucleic acid molecule consisting of the nucleotide sequence of SEQ ID NO: 45 or 46, or a complement thereof.

E⁶ 43. (Amended) An isolated nucleic acid molecule, or its complement, wherein the isolated nucleic acid i) encodes an immunogenic portion of the protein having the amino acid sequence encoded by SEQ ID NO: 46 and ii) is selected from the group consisting of:

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a) a nucleic acid molecule having a nucleotide sequence which is at least 90% identical to the nucleotide sequence of SEQ ID NO: 45 or 46;

b) a nucleic acid molecule comprising a fragment of SEQ ID NO: 45 or 46;

c) a nucleic acid molecule which encodes a polypeptide comprising the amino acid sequence encoded by SEQ ID NO: 46;

d) a nucleic acid molecule which encodes a fragment of the amino acid sequence encoded by SEQ ID NO: 46; and

E6
e) a nucleic acid molecule which encodes a variant of the amino acid sequence encoded by SEQ ID NO: 46, wherein the nucleic acid molecule hybridizes over its full length in 6× sodium chloride/sodium citrate (SSC) at about 45°C, followed by one or more washes in 0.2× SSC, 0.1% SDS at 50°C with a portion of a nucleic acid molecule consisting of the nucleotide sequence of SEQ ID NO: 45 or 46.

44. (Amended) The isolated nucleic acid molecule of claim 43, or its complement, wherein the molecule hybridizes over its full length in 6× SSC at about 45°C, followed by one or more washes in 0.2× SSC, 0.1% SDS at 50°C with a nucleic acid molecule consisting of the nucleotide sequence of SEQ ID NO: 45 or 46.

E7
54. (Amended) The isolated nucleic acid molecule of claim 43, or its complement, wherein the nucleic acid molecule encodes a variant of the amino acid sequence encoded by SEQ ID NO: 46, wherein the nucleic acid molecule hybridizes over its full length in 6× SSC at about 45°C, followed by one or more washes in 0.2× SSC, 0.1% SDS at 50°C with a nucleic acid molecule consisting of the nucleotide sequence of SEQ ID NO: 45 or 46.

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65. (Twice Amended) The method of claim 62, wherein the immunogenic portion is from a variant of the polypeptide encoded by SEQ ID NO: 46, wherein the polypeptide

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is encoded by a nucleic acid molecule which hybridizes over its full length in 6× SSC at about 45°C, followed by one or more washes in 0.2× SSC, 0.1% SDS at 50°C with a nucleic acid molecule consisting of the nucleotide sequence of SEQ ID NO: 45 or 46, or a complement thereof.

Rejection of Claims 33, 38, 40, 43-65

Pursuant to 35 U.S.C. § 112, Second Paragraph

The Examiner rejected claims 33, 38, 40, 43-65 pursuant to the second paragraph of 35 U.S.C. § 112, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The rejection with respect to claims 33, 43, 54, and 65 is described below,

Claim 33 has been amended in such a way as to obviate the insufficient antecedent basis assertion by the Examiner.

Applicants respectfully traverse the indefiniteness rejection of claims 43, 54, and 65. Despite the contentions of the Examiner, Applicants do not see as mutually exclusive (i) the preamble "encodes an immunogenic portion of the protein having the amino acid sequence encoded by SEQ ID NO: 46;" and (ii) the limitation "encodes a variant of the amino acid sequence encoded by SEQ ID NO: 46."

Protein variants are described in the present specification beginning at least on page 88, line 5. That section describes variants as having "an altered amino acid sequence which can function as either agonists (mimetics) or as antagonists," but nowhere does it say that said alterations necessarily alter the polypeptides of the invention or fragments thereof *in such a way as to impair their immunogenic characteristics*. In fact protein variants which are capable of acting as agonists "can retain substantially the same, or a subset, of the biological activities of the naturally occurring form of the protein." Therefore, it stands to reason that, although not *impossible*, it is unlikely that a TANGO 294 protein variant which is capable of serving as an agonist would be sufficiently altered to lose the immunogenic ability of the naturally occurring form of TANGO 294.

Page 89, line 28 of the present specification describes how to use polypeptides of the invention, *or fragments thereof*, as immunogens, to generate antibodies using standard

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techniques well known in the art. It stands to reason that, as long as a portion of the TANGO 294 protein was used as an immunogen (e.g., a hydrophilic region such as an epitope), it wouldn't matter whether said portion was derived from a TANGO 294 naturally occurring or variant protein- *either way, it still elicits an immunogenic response.*

A person of ordinary skill in the art recognizes that many variants of the TANGO 294 protein (e.g., that encoded by SEQ ID NO: 46) still may retain immunogenic portions of the TANGO 294, as long as the protein sequence is not altered at said immunogenic portions in such a way as to render them incapable of eliciting a TANGO 294-specific response. In fact, a person of ordinary skill in the art surely recognizes that TANGO 294 protein variants are capable of eliciting a TANGO 294-specific response *as long as even one immunogenic portion is unaltered and retains its immunogenic ability.*

Claim 43, part e), for instance, reads on a nucleic acid sequence which (1) hybridizes to a nucleic acid molecule with the sequence of SEQ ID NO: 45 or 46 under the listed stringent hybridization conditions; (2) encodes a variant of the amino acid sequence encoded by SEQ ID NO: 46 (e.g., a variant of the TANGO 294 protein, as defined in the present specification); and (3) encodes an immunogenic portion of the protein encoded by SEQ ID NO: 46. In other words, claim 43, part e) will read on a nucleic acid which encodes a TANGO 294 protein variant, and which is capable of the described hybridization, *as long as the variant is* (in the Examiner's words) *"also capable of eliciting an immune response specific to the TANGO 294 polypeptide."*

Claim 65 has been amended in such a way as to obviate the insufficient antecedent basis assertion by the Examiner.

Based on the above, Applicants respectfully request that the Examiner reconsider and withdraw the indefiniteness rejection of claims 33, 38, 40, and 43-65.

Rejection of Claims 27, 28, and 31 Pursuant to 35 U.S.C. § 112, First Paragraph

The Examiner rejected claims 27, 28, and 31 pursuant to the first paragraph of 35 U.S.C. § 112, for not enabling a person of skill in the art to use the invention commensurate in scope with the rejected claim. The Examiner in particular asserts that fragments of 25 amino acids in size (found in, for example, claim 31) are unlikely to possess the lipase activity of the present invention. In the words of the Examiner, "Therefore, it is unpredictable such a small fragment

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would possess the biological activity, thus undue experimentation would be required prior to using the claimed invention." Applicants respectfully disagree, and traverse the rejection.

The present specification (at least on page 61, line 19) describes domains found within the TANGO 294 protein sequence by using amino acid sequence comparison software and databases containing sequences that constitute regions of known activity (e.g., PROSITE database and the Hidden Markov Models database)(these domains are summarized in TABLE X). As determined by said sequence comparisons, the TANGO 294 protein is known to contain a **Lipase serine active site** from residues 180-189 (of SEQ ID NO:47).

Applicants have enclosed a several pages' worth of printouts from websites on which PROSITE information may be obtained, including from the The ExPASy (Expert Protein Analysis System) proteomics server of the Swiss Institute of Bioinformatics (SIB)(<http://us.expasy.org/prosite/>). These printouts provide details about the lipase serine active site of TANGO 294, including a long list of sequences (and their accession numbers) which also share the lipase serine active site consensus sequence. This active site, according to the PROSITE database, "is also present in lipases of prokaryotic origin, and in lecithin-cholesterol acyltransferase [...] *which catalyzes fatty acid transfer between phosphatidylcholine and cholesterol*. We have built a pattern from that region."

Thus Applicants have provided an example of at least one "small portion of a large enzyme molecule" (in the Examiner's words) that is capable of catalytic activity. Persons of ordinary skill in the art can easily determine which protein fragments and variants of the invention, regardless of their size, possess a TANGO 294 activity (e.g., a lipase activity), and are therefore within the scope of the present claims.

The Applicants respectfully request that the Examiner reconsider and withdraw the enablement rejection of claims 27, 28, and 31.

Rejection of Claims 1, 3-7, 12, 26, 30, 32, 33, 34, 36-44, 47, 51, 53, 54, 56-62, 64, and 65

Pursuant to 35 U.S.C. §§ 102 and 103

The Examiner has rejected claims 1, 3-7, 12, 26, 30, 32, 33, 34, 36-44, 47, 51, 53, 54, 56-62, 64, and 65 under 35 U.S.C. §§ 102 and 103, in view of the Blanchard reference, the Anderson reference, or a combination thereof, on the grounds that the present claims read on the

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sequences disclosed in the same because of the hybridization language. Applicant has amended claims 1, 32, 37, 39, 43, 44, 54, and 65 to include the language "over its full length," thereby obviating the rejection with respect to those claims and any depending therefrom. In other words, the hybridization is required to occur over the length of the nucleic acid molecule of the claim (even though there may be areas in which there is not complete annealing between the strands). Since the Blanchard and Anderson sequences *have only specific regions* in which there is a high enough % homology to be within the scope of the rejected claims, adding the limitation "over its full length" safely puts those sequences outside said scope (i.e., because the Blanchard and Anderson sequences do not have the requisite degree of sequence homology *over the length of the nucleic acid being hybridized*).

Summary

The Applicants respectfully contend that each of claims 1-7, 12, and 24-66 is in condition for allowance. Reconsideration and allowance of all of these claims are respectfully requested at the earliest possible time. Entry of the remarks made herein is respectfully requested.

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Respectfully submitted,

MILLENNIUM PHARMACEUTICALS, INC.

By


Paul J. Paglierani

Registration No. 52,498
75 Sidney Street
Cambridge, MA 02139
Telephone - 617-761-6865
Facsimile - 617-551-8820